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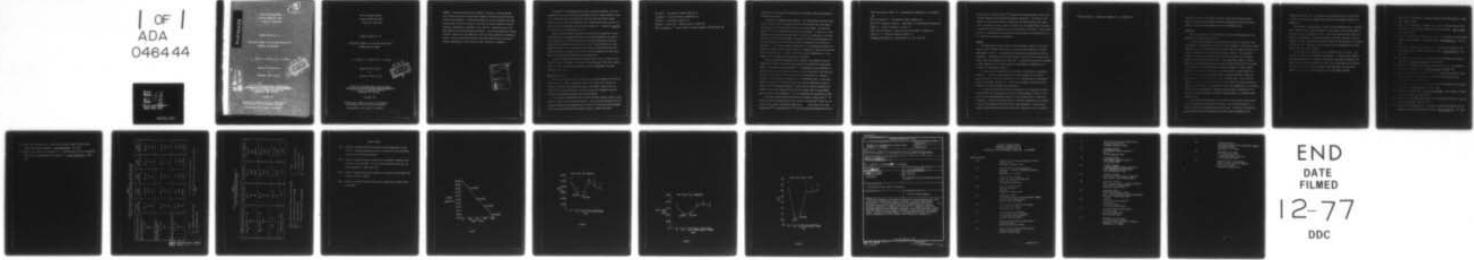
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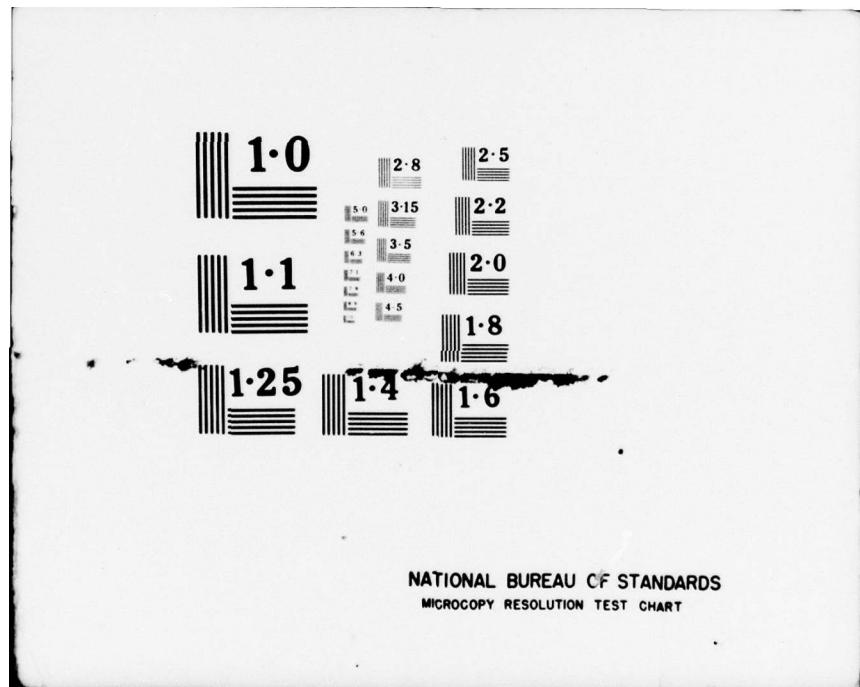
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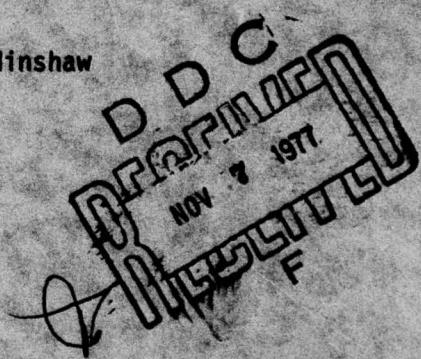
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Prepared for Publication

in

Laboratory Animal Science



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University of Oklahoma Health Sciences Center

~~Department of Pathology and Physiology~~

Division of Comparative Medicine

Oklahoma City, Oklahoma

4 October 1977

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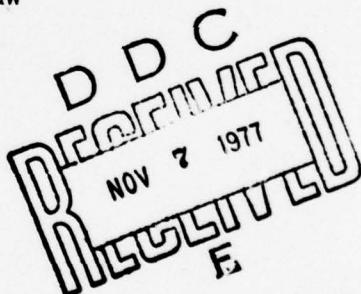
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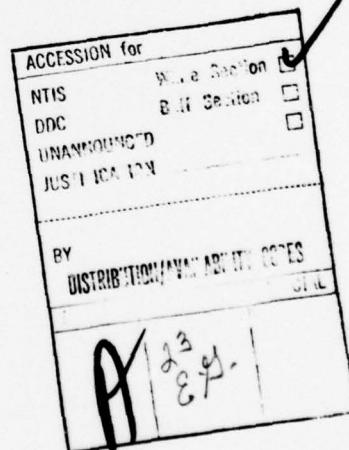
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SUMMARY. Enflurane anesthesia with thiamylal induction in the dog produced only slight, statistically insignificant, changes in the heart rate and the mean systemic blood pressure. A significant depression of the respiratory rate with an associated significant increase in the arterial partial pressure of CO<sub>2</sub> was produced, accompanied by a decrease in the blood pH. Progressive drop of the body temperature occurred throughout anesthesia. Significant hematologic changes included a reduction in the packed cell volume and the erythrocyte and leukocyte counts. The only significant change in the blood chemistry was an increase in alkaline phosphatase at 24 and 48 hours after induction of anesthesia.



Enflurane<sup>6</sup> is a nonflammable fluorinated inhalation anesthetic initially approved for use in man in 1972 and now widely used as a human anesthetic agent. It is reported to have little effect on the pulse rate and cardiac rhythm. Arterial pressure decreases moderately after induction and returns to near normal on surgical stimulation and then becomes stable (1). A precision vaporizer is necessary for safe administration (2).

Recently there has been increased concern about the occupational hazards for operating room personnel when certain inhalation anesthetics are used (3). Toxic metabolites of biotransformation of fluorinated anesthetics have been associated with hepatic and renal toxicity (4,5). Biotransformation of toxic metabolites occurs to a significantly lesser extent with enflurane than with either halothane or methoxyflurane and thus would be expected to be less hazardous to both patients and operating room personnel (6).

In view of enflurane's desirable characteristics in man, a study was conducted to determine changes in the systemic blood pressure, heart rate, respiratory rate, body temperature, blood gases, blood pH, hematology, and blood chemistry in the dog.

#### MATERIALS AND METHODS

Six healthy mongrel dogs, four females and two males weighing 10.0-18.5 kg, were used in this study. Forty-eight hours prior to the first sampling, an indwelling catheter<sup>7</sup> was surgically placed in the femoral artery utilizing thiamylal<sup>8</sup> for anesthesia so as to allow easy access at subsequent times for arterial blood samples and blood pressure measurements.

A two-channel recorder<sup>9</sup> was used to record the mean systemic arterial blood pressure, heart rate, and electrocardiogram. Heart rate was determined from the electrocardiogram, body temperature was recorded on a precision remote thermometer<sup>10</sup>, and respiratory rate was recorded visually. Blood for arterial

<sup>6</sup>Ethrane R. Ohio Medical Products, Madison, WI.

<sup>7</sup>Longdwell R. Becton-Dickinson, Rutherford, NJ.

<sup>8</sup>Surital R. Parke-Davis, Detroit, MI.

<sup>9</sup>Sanborn R, Model 7721. Hewlett Packard, Waltham, MA.

<sup>10</sup>Tele Thermometer R. Yellow Springs Instrument Company, Yellow Springs, OH.

blood gases and blood pH was collected from the femoral artery and measured on a blood gas analyzer.<sup>11</sup>

Two levels of anesthesia were studied: 2.2% vaporization during the first hour of anesthesia and 3.3% vaporization during the second hour, with oxygen flow rates of 500 ml/minute with a circle semi-closed system. The precision vaporizer<sup>12</sup> used was specifically designed for enflurane. It delivers a linear concentration of enflurane at flow rates of 0.3-10.0 liters/minute at room temperatures of 60-90<sup>0</sup>F (15.6-32.2<sup>0</sup>C). The level of 2.2% was chosen because this has been determined to be the minimum alveolar concentration for enflurane in the dog (7). The minimum alveolar concentration is the anesthetic concentration required to prevent gross muscular movement in response to a painful stimulus (8). The 3.3% concentration, 1.5 times the minimum alveolar concentration, is considered to be a moderate level of surgical anesthesia.

Prior to induction of anesthesia with thiamylal, the indwelling arterial catheter was exposed and arterial blood samples were obtained for blood gases, blood pH, hematology and blood chemistry. The cathether was also attached to the recorder and blood pressures and heart rates were obtained in the awake dog. Anesthesia was induced with 4% thiamylal given intravenously at a dosage of 16 mg/kg. The dog was then intubated with an endotracheal tube. A veterinary anesthesia machine<sup>13</sup> in combination with the precision vaporizer was used to administer the enflurane and oxygen. The dogs were in lateral recumbancy and indirect contact with the metal surface of the surgery table with no attempt made to maintain body temperature. The room temperature was maintained at 24<sup>0</sup>C.

Hematological values were determined by an automatic blood counter.<sup>14</sup> All blood chemistry determinations were done with an auto analyzer<sup>15</sup> except for the serum glutamic pyruvic transaminase determination which was done with a spectrophotometer<sup>16</sup> utilizing test kits,<sup>17</sup> and the blood glucose determination which

11 Blood Gas Analyzer, Model 113. Instrumentation Laboratory, Inc, Lexington, MA.

12 Ethrane Vaporizer <sup>R</sup>. Ohio Medical Products, Madison, WI.

13 Model 970 <sup>R</sup> Anesthesia Machine. Pitman-Moore, Inc., Washington Crossings, NJ.

14 Model Z<sub>F</sub>. Coulter Electronics, Hialeah, FL.

15 SMA 12/60 and SMA 6/60. Technicon Industrial Systems, Tarrytown, NY.

16 Junior II A. Coleman Instruments, Maywood, IL.

17 Serosonic SGPT Test Kit. Mallinckrodt, Inc., St. Louis, MO.

was done with a glucose analyzer.<sup>18</sup> Systemic arterial blood pressure, heart rate, and body temperature were monitored throughout anesthesia. The arterial blood samples for blood gases, blood pH, hematology, and blood chemistry were taken prior to anesthesia, after 1 hour of anesthesia at 2.2% concentration, and after 1 additional hour of anesthesia at 3.3% concentration of enflurane. Venous blood samples for hematology and blood chemistry were obtained at 24 and 48 hours and at 7 days after induction of anesthesia.

### RESULTS

The mean systemic arterial blood pressure decreased slightly at both anesthetic levels throughout the 2 hours of anesthesia when compared to the awake measurements (Table 1). The decrease was greatest during the greatest depth of anesthesia. There were no significant changes in the heart rate at either anesthetic level when compared to the awake dog. A statistically significant decrease in body temperature of all dogs occurred at both depths of anesthesia at all intervals of measurement (Figure 1).

The respiratory rate decreased significantly at both levels of anesthesia (Table 1). There was a corresponding significant increase in the arterial partial pressure of  $\text{CO}_2$  and a decrease in pH at increased levels of anesthesia and with increased time (Table 2). Significant increases in arterial partial pressure of  $\text{O}_2$  also occurred during anesthesia.

There were statistically significant decreases in the leukocyte and erythrocyte counts and in the packed cell volume during anesthesia (Figures 2,3,4), but no significant hematologic changes at 24 and 48 hours and at 7 days after anesthesia. The only significant change in the blood chemistry was an increase in alkaline phosphatase at 24 and 48 hours after anesthesia. No significant changes occurred at any time for the bilirubin, creatine, uric acid, inorganic

<sup>18</sup>Glucose Analyzer. Beckman Instruments, Inc., Fullerton, CA.

phosphorus, calcium, total protein, albumin, blood urea nitrogen, glucose, sodium, potassium, serum glutamic oxalacetic transaminase, and serum glutamic pyruvic transaminase when compared to the pre-anesthesia values.

#### DISCUSSION

The slight decrease in the mean systemic arterial blood pressure was comparable with changes found in man (1).

The significant decreases in the respiratory rate at all levels and times of anesthesia is important in view of the related increase in the arterial partial pressure of  $\text{CO}_2$ . The increased partial pressure possibly upset the carbonic acid to base bicarbonate with a resulting respiratory acidosis. The hypercapnia reflects a respiratory depression from enflurane, resulting in an increased arterial partial pressure of  $\text{CO}_2$  level. This respiratory acidosis, although common with general anesthetics, could possibly effect the survival of an animal if the acidosis were compounded with a metabolic acidosis. A more frequent flushing of the gas mixture through the overflow valve, a higher oxygen flow rate, or assisted ventilation would probably decrease the partial pressure of  $\text{CO}_2$  and bring the arterial pH into a more reasonable range. The significant increase in arterial partial pressure of  $\text{O}_2$  that occurred is because oxygen was used as the carrier gas. The progressive drop in body temperature with increased time and depth of anesthesia is probably caused by either a depression of the temperature regulating center, peripheral vasoconstriction, or depressed basal metabolism (9).

Muscle twitching occurred only in one dog in a pilot study in which induction of anesthesia with enflurane was by mask. This has been reported in a previous study of enflurane with induction by mask. That report indicated the muscle twitching could be prevented with either narcotic premedication or

thiopental induction (10). Since muscle twitching did not occur in any of the six dogs in this study, it appears that induction with thiamylal prevents its appearance.

The decrease in the packed cell volume and the erythrocyte count is possibly due to sequestration of the erythrocytes in the spleen as this has been shown in studies with other anesthetics (11,12). These other studies did not reveal the fate of the leukocytes. Inhalation anesthetics have been reported to cause an increase in plasma volume which would also account for the decrease in the packed cell volume (13). The cause of the elevated alkaline phosphatase at 24 and 48 hours after induction is unknown.

At the present time enflurane is not approved for use in the dog. Thus, its use is limited to the biomedical investigator. If used, minimal changes in the mean systemic arterial pressure and the heart rate should be expected and controlled ventilation to provide a pH more close to the normal of 7.4±.05 may be indicated. As with other anesthetics, body heat should be conserved by covering the animal or adding supplemental heat from water blankets.

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Effects of Enflurane Thiamylal Anesthesia on Heart Rate, Mean Systemic Arterial Pressure, and Respiratory Rate in Dogs

Time/Enflurane Concentration	Awake (Zero Time)	2.2% (30 Min.)	2.2% (60 Min.)	3.3% (90 Min.)	3.3% (120 Min.)
<b>Heart Rate (beats/min.):</b>					
$\bar{x} \pm SE$	108 $\pm$ 9	120 $\pm$ 15	110 $\pm$ 13	105 $\pm$ 7	103 $\pm$ 6
% $\Delta$	NA	+ 11.1	+ 1.9	- 2.8	- 4.3
P	NA	NS	NS	NS	NS
<b>Mean Systemic Arterial Pressure (mm Hg):</b>					
$\bar{x} \pm SE$	112 $\pm$ 7	108 $\pm$ 10	105 $\pm$ 10	104 $\pm$ 10	95 $\pm$ 10
% $\Delta$	NA	- 3.6	- 6.3	- 7.1	- 15.2
P	NA	NS	NS	NS	NS
<b>Respiratory Rate (resp./min.):</b>					
$\bar{x} \pm SE$	23 $\pm$ 2	9 $\pm$ 1	9 $\pm$ 1	7 $\pm$ 1	7 $\pm$ 1
% $\Delta$	NA	60.9	60.9	69.6	69.6
P	NA	< 0.001	< 0.005	< 0.005	< 0.005

$\bar{x}$  = mean

SE = standard error of the mean

%  $\Delta$  = percentage change

P = P value for t test for paired data

NS = not significant (P > 0.05) by t test for paired data

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TABLE 2  
Effect of Enflurane Thiethyl Anesthesia on  
Arterial Blood Gases and pH in Dogs

Time/Enflurane Concentration	Awake (Zero Time)			2.2% (+ 60 Min.)			3.3% (+ 120 Min.)		
$\text{PaCO}_2$ (mm Hg) $\bar{x} \pm \text{SE}$	34 $\pm$ 1			52 $\pm$ 3			64 $\pm$ 4		
% $\Delta$				+ 52.9			88.2		
P				NA			$< 0.001$		
$\text{PaO}_2$ (mm Hg) $\bar{x} \pm \text{SE}$	82 $\pm$ 2			406 $\pm$ 12			418 $\pm$ 10		
% $\Delta$				387.8			409.8		
P				NA			$< 0.001$		
pH $\bar{x} \pm \text{SE}$	7.43 $\pm$ .01			7.30 $\pm$ .00			7.23 $\pm$ .00		
P				NA			$< 0.001$		
Base Excess (m Eq/L)	- 0.75			- 1.80			- 2.80		

$\text{PaCO}_2$  = arterial partial pressure of carbon dioxide

$\text{PaO}_2$  = arterial partial pressure of oxygen

pH = pH of arterial blood

P = P value for t test for paired data

$\bar{x}$  = mean

SE = standard error of mean

%  $\Delta$  = percentage change

NA = not applicable

#### FIGURE LEGENDS

Fig 1. Effect of thiamylal-enflurane anesthesia on body temperature of dog (in  $^{\circ}\text{C}$ ). Enflurane concentration was 2.2% during the first 60 minutes and 3.3% during the next 60 minutes

Fig 2. Effect of thiamylal-enflurane anesthesia on peripheral leukocyte count of dog (in cells per  $\text{mm}^3$ ). From the 2nd hour through the 7th day, no other anesthesia or agents were used.

Fig 3. Effect of thiamylal-enflurane anesthesia on peripheral erythrocyte count of dog (in cells  $\times 10^6/\text{mm}^3$ ).

Fig 4. Effect of thiamylal-enflurane anesthesia on packed cell volume of dog (in percent).

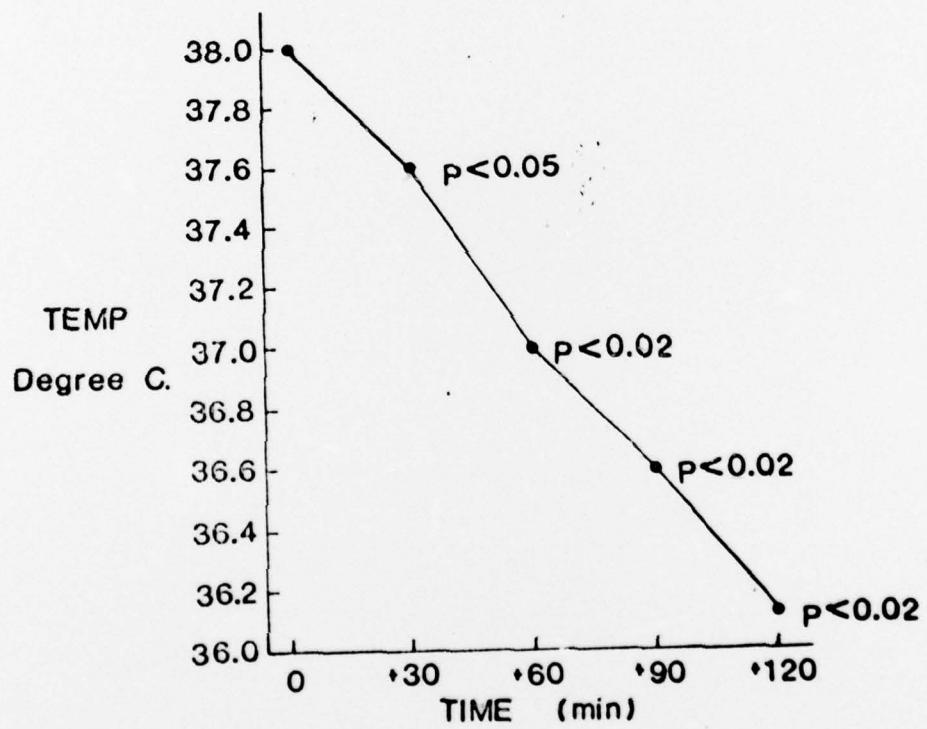


FIGURE 1

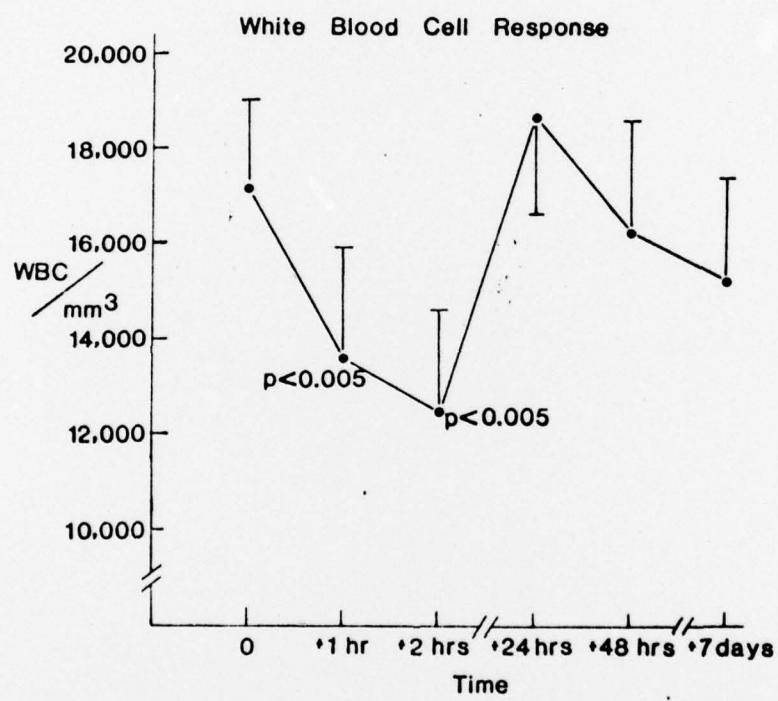


FIGURE 2

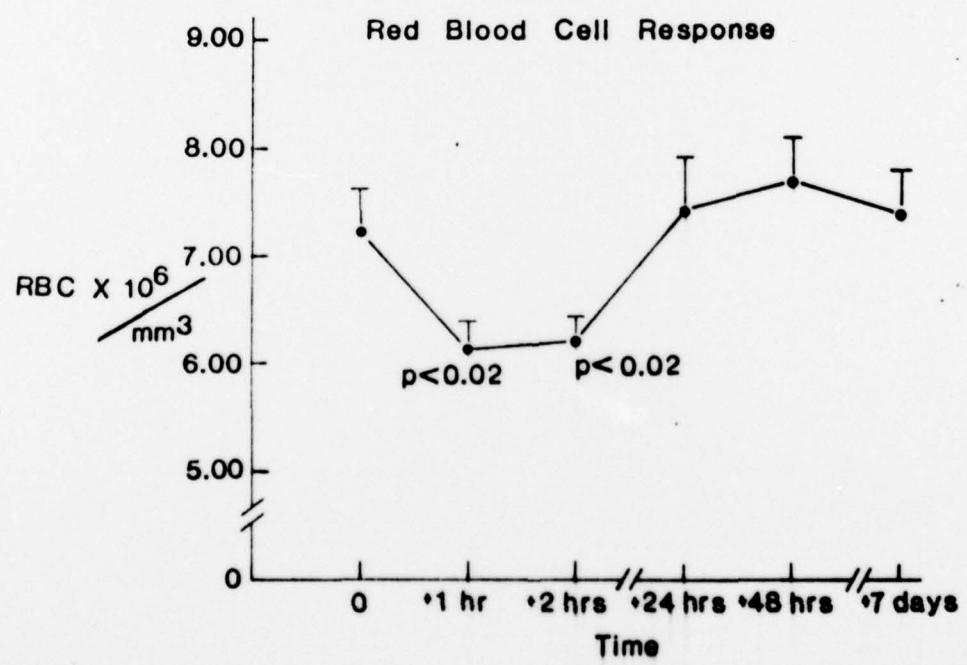


FIGURE 3

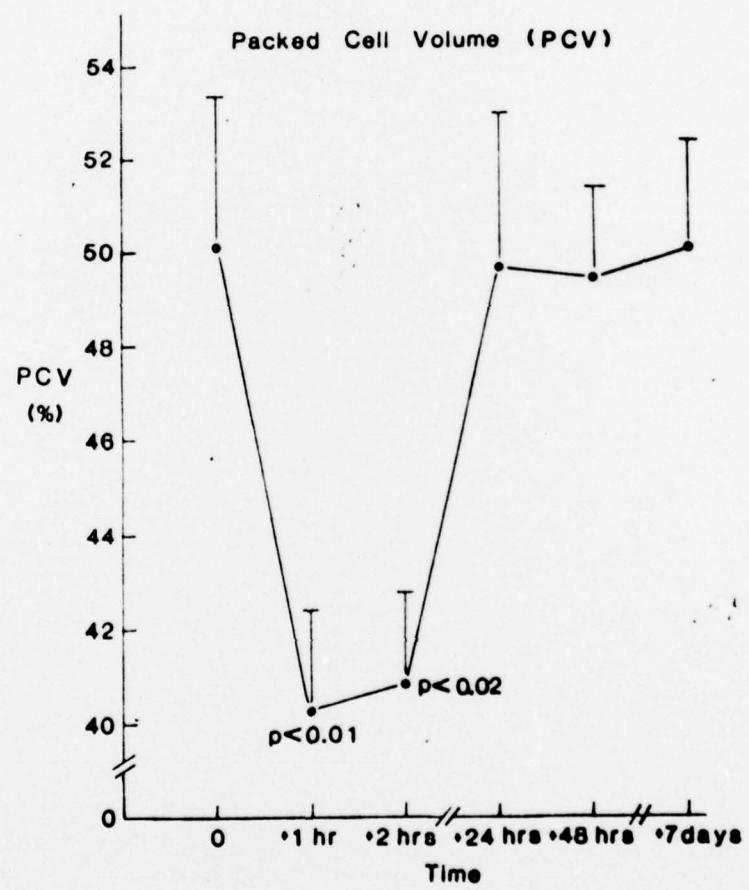


FIGURE 4

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